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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,639	06/26/2001	Randolph J. Noelle	P 0280639	9079

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,639	NOELLE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7-11,13-15,17,20,21,24-26,28-31,34,35,38-43 and 46-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, 7-11, 13-15, 17, 20, 21, 24-26, 28-31, 34, 35, 38-43, 46-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 7/3/04, has been entered.

Applicant's amendment, filed 7/3/04, has been entered.
Claims 1, 15, 30 and 42 have been amended
Claims 2-3, 5-6, 12, 16, 18-19, 22-23, 27, 32-33, 36-37, 44-45 have been canceled.

Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-43 and 46-50 are under consideration in the instant application.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 7/3/04.
The rejections of record can be found in the previous Office Actions.

3. Upon reconsideration of applicant's amended claims, filed 7/3/04, the previous rejection under 35 U.S.C. 112, first paragraph with respect to the recitation of "tolerance" has been withdrawn.

4. Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-43 and 46-50 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lederman et al. (U.S. Patent No. 6,403,091) in view of Berschorner (U.S. Patent No. 5,597,563) and Cobbold et al. (U.S. Patent No. 6,056,956) essentially for the reasons of record.

Applicant's arguments, filed 7/3/04, have been fully considered but are not found convincing essentially for the reasons of record set forth in the previous Office Actions.

Applicant argues that the combination of references would not have given any incentive to induce T cell non-responsiveness to an allogeneic or xenogeneic donor tissue or organ in a human recipient comprising administering a donor cell and an anti-human gp39 antibody.

It is noted that human soluble CD40 is no longer being claimed.

Applicant asserts that Lederman et al. describes antibodies to an uncharacterized antigen (5c8) present on activated by not resting T cells, which antibody inhibited T cell activation of B cells.

Applicant is reminded that Lederman et al. do teach the use of 5C8-specific (CD40L-specific) antibodies to inhibit the rejection of transplanted tissues (see column 11, paragraph 6) as well as claim methods of inhibiting rejection of transplant organ in humans with 5c8-specific antibodies (see Claims).

Applicant argues that the mechanism of tolerance achieved using the non-depleting anti-CD4 and anti-CD8 antibodies would provide no motivation to substitute an anti-gp39 antibody to achieve tolerization

Applicant further asserts that the teachings of using non-depleting antibodies by Cobbold would teach away form the use of antibodies that induce T cell non-responsiveness by ablation, as done by the anti-gp39 antibodies of the claimed invention.

Applicant asserts that Cobbold's teachings are irrelevant to anti-gp39 antibodies, since these teachings cannot be randomly extrapolated to antibodies against any T cell antigen, particularly to antibodies against gp39 which were believed to only inhibit the T cell's activation of a B cell.

Applicant further asserts that Cobbold et al. further describe the development of a regulatory T cell populations elicited through the non-depleting antibodies (see Table 5 on column 19, lines 23-43 of Cobbold et al.). Here, applicant submits that the data in Table 5 show that transfer of normal spleen cells could not break tolerance unless recipient CD4+ T cells were depleted first (e.g. see column 13, lines 4-12 of Cobbold et al.).

Applicant note that Cobbold's discovery of the effects of non-depleting antibodies which appear to elicit a regulatory T cell population defied conventional wisdom (see Waldmann, Immunol. Rev. 185: 227-235, 2002).

As pointed out previously, Cobbold et al. teach methods of preventing graft rejection in tissue and organ transplants with anti-T cell antibodies in order to induce tolerance by providing antigen (see entire document, including columns 1-4). Cobbold et al. teach the provision of the antigen and the immunosuppressant at different times to provide an tolerance-permissive environment (see column 1-4).

However, Cobbold teach both depleting and non-depleting antibodies to T cells, including T helper cells as potent immunsuppressive agents in controlling transplant rejection (see entire document, particularly columns 1-3).

Furthermore, Cobbold et al. teach administering immunosuppressive antibodies prior to commencement of even the non-depleting CD4 and CD8 antibodies regimen (see column 3, paragraph 7 - column 4, paragraph 3) to indicate the obviousness of providing immunosuppressive antibodies prior to transplantation to establish an immunosuppressive environment.

While applicant asserts that the dissimilarities between CD4 and gp39 further distinguish the present invention, Lederman et al. provides sufficiint motivation and expectation of success that 5c8-specific antibodies that bound and inhibited T cell-mediated responses were useful immunosuppressant agents and more specifically, immunosuppressant agents in the treatment of transplant recipients.

Although the references and instant application may have disclosed alternative mechanisms of action in tolerance induction, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145.

On this record, it is reasonable to conclude that the same patient (e.g. transplant recipients) is being administered the same active agent ((e.g. anti-gp39 / anti5c8 / anti-CD40 ligand antibodies) by the same mode of administration in the same amount in both the instant claims and the prior art reference. The fact that applicant may have discovered yet another beneficial effect from the method set forth in the prior art does not mean that they are entitled to receive a patent on that method.

Remember obviousness can be established for achieving the claimed product for different reasons and the prior art/examiner does not need to know all of the properties of the claimed invention In re Dillon, 16 USPQ2d 1897 (Fed. Cir. 1990); however there must be some suggestion or motivation. Therefore, the reason or motivation to combine may often suggest doing what the inventor has done, but for a different purpose or to solve a different problem than that asserted by the inventor. See MPEP 2144.

A prior art reference may be considered to teach away when "a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant." See In re Gurley , 31 USPQ2d 1130, 1131 (Fed. Cir. 1994).

Here in contrast to applicant's assertions of teaching away by the prior art because the references provide alternative methods of tolerance induction or explanations of mechanisms of action; there is no discouragement nor skepticism in the prior art for employing anti-5c8 (i.e. anti-gp39, anti-CD40 ligand) antibodies as an immunosuppressant and more specifically as an immunosuppressant to inhibit transplant rejection.

Applicant's reliance on differences in mechanisms of actions, including further investigations post-filing date, does not negate the clear motivation and expectation of success that anti-5c8 (i.e. anti-gp39 anti-CD40 ligand antibodies) were considered immunosuppressant agents to inhibit graft rejection and were not limited to inhibiting B cell responses, as asserted by applicant.

Applicant asserts that anti-gp39 antibody would have deleterious effects on Bershorner's tolerization process, given the critical timing of the immunosuppressive treatment and APC recruitment or infusion (e.g. see column 5, lines 13-20). Applicant asserts that Berschorner teaches that the immunosuppressant should not be present when the new APCs start presenting their antigen or autoantigen to T cells, which leads to subsequent T cell activation and gp39 presentation. Applicant submits that anti-gp39 antibody would have no effect prior to administration of desired APCs to induce tolerance, if used as an immunosuppressant according to Berschorner, as no relevant gp39 expressing T cells are present prior to administration of APCs. Applicant also submits that anti-0gp39 antibodies would have a deleterious effect on the APCs since they block gp39 binding to CD40, the very thing Berschoner warns against.

In contrast to applicant's limited reading of Berschorner, again Berschorner teach methods of inducing antigen-specific immune tolerance by providing antigen presenting cells containing the antigen to which specific tolerance is desired (see entire document, including Background of the Invention, including column 2, paragraph 2, Detailed Description of the Invention). Berschorner also teach that the antigen presenting cells, which can be isolated from a number of hemopoietic tissues and can include dendritic cells, Langerhans cells and mononuclear phagocytes (e.g., see column 6, paragraphs 3-4) would be administered with an immunosuppressant agent contemporaneously with the antigen presenting cells (see Detailed Description of the Invention, including column 8, column 4). Both alloantigens and xenoantigens are targeted (see columns 5, paragraph 4 - column 6, paragraph 1), including the treatment of a number of diseases (see column 6, paragraph 2).

While Berschorner may have described alternative methods of inducing tolerance to antigens of interest, Beschorner et al. stands for the use antigen presenting cells containing the antigen in methods of inducing antigen-specific immune tolerance to an antigen to which specific tolerance is desired.

In contrast to applicant's assertions and given the teachings of providing antigen and/or antigen presenting cells containing the antigen to which specific tolerance is desired, including those at the time transplant, contemporaneously with immunosuppressants, as taught by Berschorner and/or Cobbold; one of ordinary skill in the art would have been motivated to combine the immunosuppressive properties of the CD40L-specific antibodies, taught by Lederman et al., to create an environment conducive to tolerance or specific unresponsiveness in the transplantation of a number of tissues and organs at the time the invention was made.

In contrast to applicant's assertions and given the teachings of Cobbold et al. that the presence of antigen as well as the use of anti-T cell antibodies can provide an environment conducive to tolerance or specific unresponsiveness, one of ordinary skill in the art would have had a reasonable expectation of success and motivation to employ the CD40L-specific antibodies in combining antigen presenting cells in transplanting a variety of tissues and organs at the time the invention was made.

Given the prior art teachings of inducing nonresponsiveness to both alloantigens and xenoantigens as well as the use of a variety of antigen presenting cells to a variety of transplanted tissues and organs, one of ordinary skill in the art would have employed a variety of antigen presenting cells, including those encompassed by the instant claims as known antigen presenting cells, particularly the ready availability of human B cells as antigen presenting cells at the time the invention was made. Also, transplanting a number of tissues and cells, including those encompassed by the instant claims was known and practiced by the ordinary artisan at the time the invention was made.

In contrast to applicant's arguments, the prior art provides sufficient teachings, motivation and expectation of success in targeting the same T cells with the same gp39- / CD40L-/5C8- specific antibodies and antigen presenting cells to achieve the same long term graft survival in the same transplant patients at the time the invention was made.

It would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Berschorner AND/OR Cobbold et al. to those of Lederman et al. to provide methods of providing an environment conducive to tolerance or specific unresponsiveness by combining an immunosuppressant such as the CD40 ligand-specific antibodies, taught by Lederman et al. with a source of alloantigen or xenoantigen, as taught by Berschorner and Cobbold et al. to transplant a variety of tissues and cells. A person of ordinary skill in the art would have been motivated to produce this resultant therapeutic regimen to provide an environment conducive to tolerance or specific unresponsiveness to decrease the rejection of the transplanted tissue or organ and to increase the survival of such transplants. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

6. Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-43 and 46-50 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims 1-34 of U.S. Patent No. 5,683,693,
claims 1-34 of U.S. Patent No. 5,902,585, and
claims 1-7 of U.S. Patent No. 6,375,950

for the reasons of record.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims and the patented claims appear to read on the same or nearly the same methods of inducing specific unresponsiveness. Further, the patented claims appear to anticipate the instant methods.

Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-43 and 46-50 are directed to an invention not patentably distinct from claims 1-34 of commonly assigned U.S. Patent No. 5,683,693 and claims 1-34 of commonly assigned U.S. Patent No. 5,902,585 for the reasons set forth above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 5,683,693 and U.S. Patent No. 5,902,585, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Applicant's amendment indicates that terminal disclaimer will be filed upon clarification of the inventorship and ownership.

7. No claim allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

PHILLIP GAMBEL

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November 29, 2004